REMARKS

Claims 9-12 were pending in the present application and were rejected. Claims 9, 11 and 12 are herein amended. New claims 14-23 are added herein. No new matter has been added.

Applicants' Response to Claim Rejections under 35 U.S.C. §102

Claims 9-12 were rejected under 35 U.S.C. §102(a) and 102(e) as being anticipated by Kumta et al. (U.S. Patent Application Publication No. 2003/0219466).

As acknowledged in the Advisory Action dated February 26, 2008, the rejection based on Kumta has been withdrawn.

Claims 9-12 were rejected under 35 U.S.C. §102(a) and 102(e) as being anticipated by Doll et al. (U.S. Patent Application Publication No. 2003/0235564).

The Advisory Action dated February 26, 2008 notes that the request for reconsideration was considered but did not place the application condition for allowance because the arguments were regarded as failing to overcome the rejection of claims 9-12 under 35 U.S.C. §§102(e) and under 35 U.S.C. 102(a) as being anticipated by Doll et al.

With respect to the remarks of the Advisory Action, Applicants herein provide the following comments. First, Applicants respectfully submit that the Advisory Action mischaracterizes Applicants' position as being that "a degasified condition under a reduced pressure of 100 to 150 mmHg for 3 hours or longer is required for the claimed adsorption to occur (emphasis added)." This is inaccurate.

Rather, Applicants' position is that the reduced pressure environment necessarily gives rise to adsorption, and a high-pressure environment necessarily gives rise to non-adsorption. However, adsorption is not necessary the result of a low-pressure environment. In other words, although low-pressure environment necessary results in adsorption, as clearly stated on page 10, lines 4-7 of the Request for Reconsideration filed on January 25, 2008, other conditions may also give rise to adsorption.

On the other hand, a high-pressure environment, such as that in Doll, necessarily gives rise to non-adsorption. Examples of other conditions which give rise to non-adsorption include (i) immobilization (crosslinking) of genes to the implant by UV irradiation, and (ii) mixing bioadaptable filling such as collagen gel and alginate with genes to make an implant.

Thus, this aspect of Applicants' position can be summarized as follows:

Low-pressure → adsorption
Other, non-discussed processes → adsorption

High-pressure → non-adsorption
UV-irradiation → non-adsorption
Fillings/alginate mixing → non-adsorption

Next, the Advisory Action states that "Applicant's arguments focus on the process how the implant being made requires a specified condition. However, the Advisory Action notes that the degasified reduced pressure condition is not recited in the claim." The Advisory Action is correct in noting that the degasified reduced pressure condition is not recited in the apparatus claims. However, this degasified reduced pressure condition results in the recited adsorption. This adsorption imparts distinctive structural characteristics to the final product. Specifically, the

adsorption imparts a distinctive arrangement of the vector on the bioadaptable porous material, in which the vector is concentrated on the surface of the bioadaptable porous material.

The Advisory Action is of the position that Doll inherently discloses adsorption, and thus inherently discloses a product which is structurally identical to the claimed product. However, Applicants note that the Advisory Action did not comment on Applicants' remarks that the cells in Doll are subjected to high-pressure during the incorporation of Runx2 into the porous material, and, as a result, are not adsorbed onto a bioadaptable material.

The Advisory Action states that "[c]onsidering a pharmaceutical composition comprises β-TCP and a polynucleotide encoding Cbfa1 dissolved in water, the claimed adsorption process will inherently occur." According to MPEP § 2112:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (emphasis in original).
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> "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted) (emphasis added).

In other words, in order to rely on the inherency argument, it must be shown that adsorption necessarily occurs in Doll. As explained above, Applicants respectfully submit that adsorption does not necessarily occur in Doll.

A vector may be incorporated into a bioadaptable material by various alternative incorporation schemes. One such incorporation scheme is adsorption of the vector on the bioadaptable material. Whether adsorption will occur depends on the conditions present. As explained above, some conditions will give rise to adsorption and some will not.

Doll is silent with respect to how the Runx2 plasmid is incorporated into a bioadaptable material. However, as discussed above, specific procedures must be undertaken in order to ensure adsorption. However, Doll does not disclose or suggest these required procedures. Rather, Doll describes at paragraph [0067] that:

> injecting a suspension of cells in a polymer solution improves the reproducibility of cell seeding throughout a device, and protects the cells from shear forces or pressure induced necrosis, and aids in defining the spatial location of cell delivery. (emphasis added).

In other words, the cells are subjected to a high pressure during the course of incorporating the Runx2 into the porous material. As such, adsorption cannot occur.

On the other hand, as explained in the Request for Reconsideration filed on January 25, 2008, the specification achieves adsorption by using a low-pressure condition. However, other experimental conditions could give rise to adsorption.

Applicants additionally note the discussion of product-by-process claims in the Advisory Action. As noted by the Advisory Action, the determination of patentability is based on the product itself, as explained in MPEP § 2113. MPEP § 2113 also states that:

> The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is

made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.

Doll discloses a high-pressure environment during the incorporation of Runx2 into the biomaterial. Since a high-pressure environment necessarily gives rise to non-adsorption, Doll cannot disclose a vector adsorbed onto a biomaterial. Since adsorption, or the lack thereof, imparts a distinctive structural characteristic on the product, the claimed product is structurally distinct from the product of Doll. Additionally, it would not have been obvious to modify Doll to adsorb the vectors onto the bioadaptable material

In addition to these structural differences, Applicants note at least the following benefits of the claimed implant. The present invention enables *in situ* sustained release of Cbfa1 gene and achieves remarkable bone regeneration. The effect of the present invention is clearly demonstrated in the examples of the specification. In addition, the bioadaptable porous material used in the present invention can be sintered to improve its strength. Also the porous material used in the present invention shows higher cell infiltration and angioinvasive properties. Therefore, for at least the above reasons, Applicants respectfully submit that Doll does not disclose or suggest the implant as recited by claims 9-12. Favorable reconsideration is respectfully requested.

New Claims

Applicants herein add new claims 14-23. New claims 14 and 21 recite the inclusion of bone-marrow derived cells in the implant. New claims 15 and 22 recite that these bone marrow

derived cells are osteoblasts. This is supported at least by the specification at page 6, line 22 to page 7, line 8. Claims 16 and 23 recite that the bone marrow derived cells are isolated from an individual in need of the implant. This is supported at least by the specification at page 10, line 24 to page 11, line 13, and page 12, lines 11-26. Additionally, claim 9 is amended to recite "comprising" instead of "consisting of." Finally, new claims 17-20 recite similar subject matter as claims 9-12, except that hydroxyapatite has been removed. No new matter has been added.

The implant of the present invention may comprise bone marrow derived cells as cell as viral vectors. Examples of the present invention show that both implants, with and without bone marrow cells, achieved excellent bone regeneration. The use of bone marrow cells with a viral vector is not disclosed or suggested in Doll. Additionally, in Doll, only hydroxyapatite is disclosed as a bioadaptable material. Accordingly, Applicants respectfully submit these new claims are patentable over the cited art. Favorable consideration is respectfully requested.

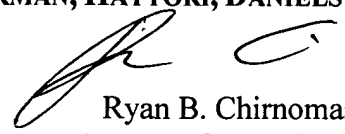
For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP



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